

b.) Remarks

Claims 25 and 72 have been amended in conformity with their antecedent claims and to correct inadvertent typographical errors. Additionally, new claims 73-80 are presented in order to more specifically recite various preferred embodiments of the present invention.

For the Examiner's convenience, the subject matter of the amendment may be found throughout the specification (e.g., the abstract as filed) as well as in claim 23 as considered on June 2, 2009. Accordingly, no new matter has been added.

Claims 23, 71 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenlee (U.S. Patent Publication No. 2003/0139395) in view of Suzuki (U.S. Patent No. 5,543,415) and Goodman & Gilman's (*The Pharmacological Basis for Therapeutics*, 10<sup>th</sup> Edition (2001) 469).

According to the Examiner, Greenlee teaches use of adenosine A<sub>2A</sub> receptor antagonists in treating anxiety-related disorders. As before, Suzuki teaches (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine and Goodman & Gilman's shows antidepressants are used to treat generalized anxiety disorders.

As discussed at page 5 of Applicants' July 6, 2009 Preliminary Amendment, specific antidepressants may be used for treating a particular anxiety disorder such as generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, agoraphobia, and social phobia. Although Goodman & Gilman's teaches that antidepressants are leading choices in treating severe anxiety disorders, including generalized anxiety disorder, social phobia and obsessive-compulsive disorder, Applicants

explained there is no basis in fact to allege that any antidepressant is useful for all such anxiety disorders.

Accordingly, Greenlee is newly-applied as teaching adenosine A<sub>2A</sub> receptor antagonists are useful in treating anxiety-related disorders in combination with antidepressants or anxiolytic agents, as well as disclosing various triazolopyrimidine compounds (see formula VII) having adenosine A<sub>2A</sub> receptor antagonistic activities although, as acknowledged by the Examiner, Greenlee does not teach Istradefylline<sup>1</sup> as the adenosine A<sub>2A</sub> receptor antagonist. Moreover, Greenlee does not disclose any data showing the effects of any adenosine A<sub>2A</sub> receptor antagonists on anxiety.

To the contrary, the test examples herein are all models of anxiety disorder (see page 61, ninth line from the bottom to page 62, line 15). As seen, test examples 1, 4 and 5 are particularly apt for generalized anxiety disorder (“GAD”).

Moreover, the present application conclusively evidence the unexpected superiority of Istradefylline over adenosine A<sub>2A</sub> receptor antagonists that are closer than those known in the prior art. For instance, from the results of test example 1, Istradefylline at 3 mg/kg po shows vastly more potent activity on the change of the number of head-dips than Compound C<sup>2</sup> (at 10 mg/kg po). (Compare Table 1-A at page 50 with Table 1-C at page 51). Similarly, test examples 4 and 6 show the effects of Istradefylline on the Elevated Plus-Maze and Social Interaction tests are vastly more potent than those of

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<sup>1</sup> (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine, see page 39.

<sup>2</sup> 5-amino-2-(2-furyl)-7-[4-(3-hydroxy-3-methylbutyl)piperazinyl][1,2,4]triazolo[1,5-c]pyrimidine, see page 40.

Compound C. (Compare Table 3-A at page 55 with Table 3-C at page 56, and Table 4-A at page 56 with Table 4-C at page 57).

As the Examiner will appreciate, Compound C is a compound having a triazolopyrimidine skeleton (see Greenlee's formula VII). Therefore, even though (i) Goodman & Gilman's teaches that antidepressants are leading candidates for treating severe anxiety disorders, (ii) Greenlee teaches that adenosine A<sub>2A</sub> receptor antagonists in combination with antidepressants or anxiolytic agents are useful in treating generalized anxiety disorder, and (iii) Suzuki teaches Istradefylline is an adenosine A<sub>2A</sub> receptor antagonist, the superiority of Istradefylline in treating of generalized anxiety disorder would not have been expected by the one of ordinary skill in the art. Thus, any *prima facie* case of obviousness is rebutted on the record herein.<sup>3</sup>

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 23, 25 and 71-80 remain presented for continued prosecution.

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<sup>3</sup> Test example 2 is a model for obsessive-compulsive disorder, the test example 4 is a model for generalized anxiety disorder, panic disorder and agoraphobia, and the test example 5 is a model for generalized anxiety disorder and social phobia. As evidenced in the specification, Istradefylline showed significantly more potent activities than Compound C in each of those test examples as well.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

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